

# Malaria Risk Assessment for the Republic of Korea Based on Models of Mosquito Distribution

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## ABSTRACT

Data on climate, environment, and adult and larval mosquito collection sites throughout the Republic of Korea (ROK) were used to model the potential distribution of the 8 anopheline species known to occur there. These models were overlaid on predicted areas of malaria suitability to better define the distribution of malaria risk in the ROK. The concept of the “mal-area”—an area of co-occurrence of humans, parasites and vectors, where malaria transmission is possible—is explained. Quantification of the mal-area in the vicinity of 5 military installations in the north of the country suggested that they had very different malaria risks, depending on what the vector species were, and the method of calculation. An online mal-area calculator for malaria risk assessment (currently under development) is discussed.

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## INTRODUCTION

Arthropod-borne pathogens that cause diseases, such as malaria, yellow fever, and dengue, are major health threats to the military. For example, losses to malaria and other preventable diseases among Allied forces operating in the China-Burma-India theater during World War II far exceeded the number of casualties inflicted by enemy action.<sup>1</sup> Malaria was second only to combat injury as the reason for hospitalization among American troops in Vietnam, and the number one reason for troops deployed to Somalia.<sup>2</sup> A significant proportion of Joint Task Force personnel inserted into Liberia in August 2003 (80 out of 290 who had been ashore) experienced symptoms of malaria.<sup>3</sup> Infected troops returning to the United States increase the rate of imported malaria.<sup>4</sup>

*Anopheles* mosquito species are solely responsible for global malaria cases. Over 450 species of *Anopheles* are known, but only a fraction are malaria vectors. More precise information on the actual and potential geographic distribution of the species responsible for malaria could assist a host of health-related actions, including predeployment counselling for prophylaxis; the choice of health messages during deployment;

decisions as to the locations of refugee camps, hospitals, and bases; postdeployment evaluation of health risk exposures; selection of the type and extent of vector control; the choice of vector identification tools; identification of the likely vector for a region; and management or quarantine of invasive vector and parasite species.

Recently, computer programs have become available that combine climate information with data on where organisms have been collected to produce maps of the potential distribution of these organisms.<sup>5,6</sup> A variety of mosquito species have been modeled in this way.<sup>7,8</sup> The output from these models, usually the suitability for occurrence of a particular species, can be extended to a resolution of one km<sup>2</sup> or less.

The zone where humans, parasites and vectors co-occur constitutes a geographic area of malaria risk that we dub the “mal-area” (see Figure 1). The mal-area can be regarded as the ecological niche or potential spatial extent of this disease.<sup>9</sup> A subset of the ecological niche is the mal-area of current transmission, which expands and contracts according to the level of mosquito survival and abundance, human-vector contact, and case detection and

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treatment, among a myriad of other factors. Because the *Plasmodium* parasite is normally dependent on a human or mosquito host, the mal-area should approximate the spatial extent of the parasite. The phenomenon of “anophelism without malaria” describes the area where vectors and humans, but not parasites, co-occur, eg, many populated parts of the United States have malaria vectors but the disease was eradicated there.

Until recently, detailed intelligence on the distribution of vectors was not available for malaria risk models. The Malaria Atlas Project<sup>10</sup> (MAP) models the limits of actual malaria transmission using information on international travel-health guidelines and estimates of vector occurrence, from altitude and degree of urbanization data.<sup>11</sup>

Fine-tuning such maps of global malaria suitability by incorporating detailed mosquito species distribution models could provide a clearer picture of areas of heightened malaria risk. The resulting mal-area extent could be used as a simple index to compare malaria risk between locations of interest (Figure 1). Specifically, mal-area mapping could improve force health protection in areas of operation such as the Republic of Korea (ROK) that have a history of malaria transmission.

Prior to the 1950s, *Plasmodium vivax* malaria was endemic and widespread in the ROK,<sup>12</sup> suggesting that the potential mal-area is extensive in that country. Malaria was eradicated in the 1970s but reemerged in 1993 and reached a peak of 4142 cases in 2000 before falling to 774 cases in 2004.<sup>13</sup> Most malaria cases appear to have been contracted near the Demilitarized Zone (DMZ) that separates North and South Korea.<sup>13</sup> This is reflected in the northerly location of the area of current malaria suitability, as determined by the MAP models (see Figure 2). The anopheline fauna of South Korea (ie, the ROK) is relatively well resolved taxonomically,<sup>14-16</sup> and ongoing mosquito surveillance makes this country an ideal location to test the mal-area approach to assessing malaria risk. The anopheline fauna of the ROK includes 8 species:

*Anopheles sinensis* sensu stricto (s.s.) Wiedemann  
*An. pullus* M. Yamada (= *An. yatsushiroensis*)  
*An. lesteri* Baisas & Hu (= *An. anthropophagus*)  
*An. sineroides* S. Yamada  
*An. kleini* Rueda  
*An. belenrae* Rueda

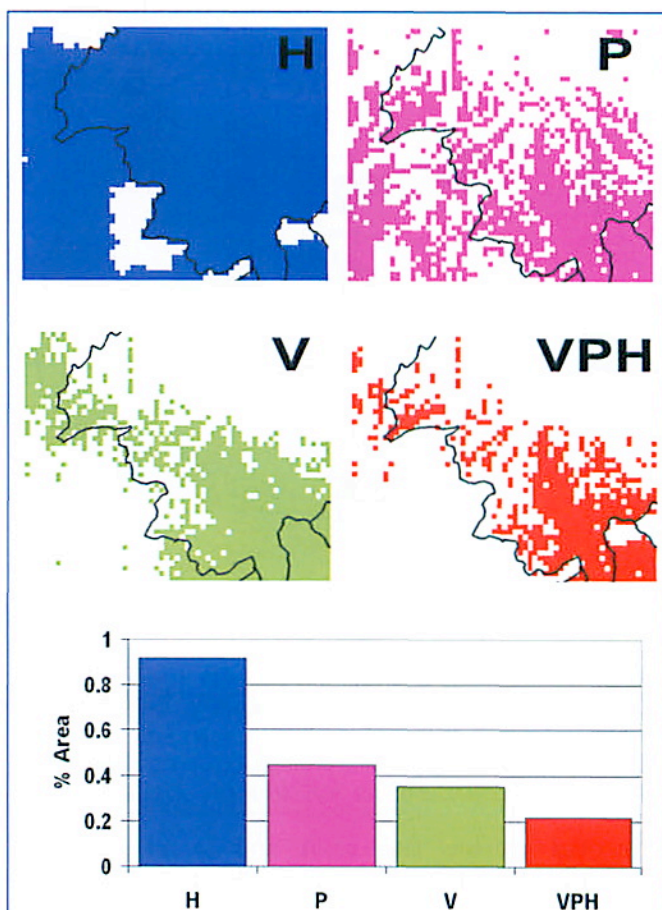


Figure 1. Illustration of the concept of the mal-area as it applies to malaria risk assessment in geographic space. Presence/absence of humans (H), areas of suitability for *Plasmodium* species (P), and predicted distribution of malaria vectors (V) are shown, as well as the mal-area (VPH); the area of overlap where malaria transmission is possible. Histogram shows the percentage of the sampled area that these parameters cover. The value for VPH could be used as a simplified index of malaria risk to compare different areas.

*An. lindesayi japonicus* S. Yamada

*An. koreicus* S. Yamada & Watanabe

These species are not all identifiable based on morphology, but a polymerase chain reaction (PCR) technique has been developed for species identification.<sup>15</sup> Historically, *An. sinensis* was considered the primary vector. However, the discovery of additional species and results from field and laboratory parasite studies have combined to point to *An. kleini*, *An. pullus*, and *An. sinensis* as the likely vectors around the DMZ.<sup>13</sup> Logically, since further mosquito and parasite sampling is required, all species could be regarded as potential vectors.



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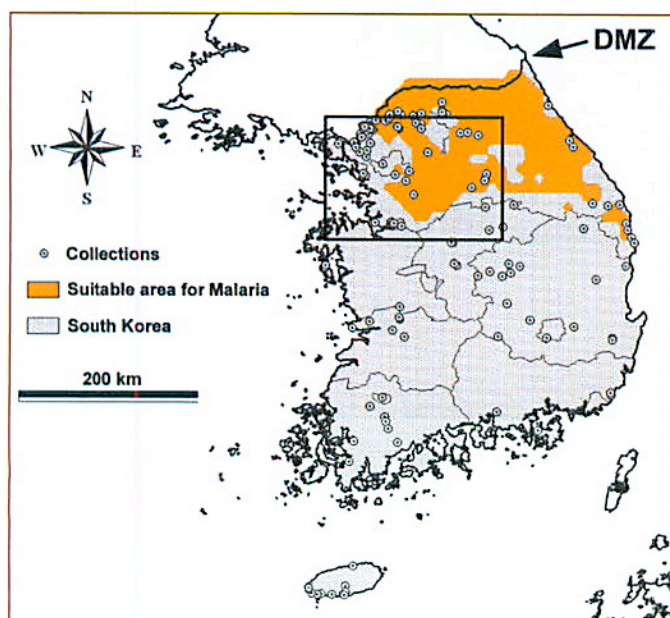


Figure 2. Locations of mosquito collection points in the ROK used in species distribution modelling. Also depicted is the extent of the area predicted active for malaria. (Data derived from the Malaria Atlas Project.<sup>10</sup> Data from the boxed area was used for mal-area calculations.

We used climate and adult and larval mosquito collection data from sites throughout the ROK to model the distribution of all 8 anopheline species. To better understand the distribution of malaria risk in the ROK, especially around military installations in the north of the country, the resulting models of potential species distributions were compared with areas of malaria suitability. An online mal-area calculator for malaria risk assessment that is under development is discussed later in this article.

### MATERIALS AND METHODS

Adult mosquito surveillance was conducted at selected US military installations using New Jersey light traps (John W. Hock Co, Gainesville, FL) and Mosquito Magnets<sup>®</sup> (Woodstream Corporation, Lititz, PA) (Figure 3), and larval collections were made throughout the ROK. Adults and larvae were identified to species by comparison of DNA products produced by PCR.<sup>15</sup>

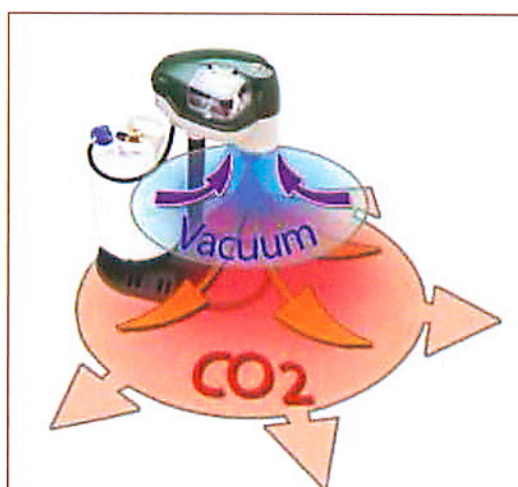


Figure 3. The Mosquito Magnet uses propane to produce CO<sub>2</sub> and heat to attract insect vectors which are caught in the vacuum and deposited in the collection bag.

We used the Genetic Algorithm for Rule-set Prediction (GARP)<sup>5,17</sup> and a maximum entropy approach, known as Maxent,<sup>6,18</sup> for distribution modelling. GARP uses an iterative process of rule selection, evaluation, testing, and incorporation or rejection. The genetic algorithm in GARP allows the rules to “evolve” to maximize predictive accuracy. A rule is selected and is applied to half the points (training data) and models assessed with the other half of the points (testing data). The change in predictivity between iterations is used to evaluate whether a particular rule should be incorporated into the model. Maxent is based on the idea that the best explanation for unknown phenomena will maximize the entropy of the probability distribution, subject to the constraint of the environmental conditions where species have been detected. Output was predicted probability of presence. The methodology and results of this modelling will be reported in greater detail in a forthcoming paper.

We obtained

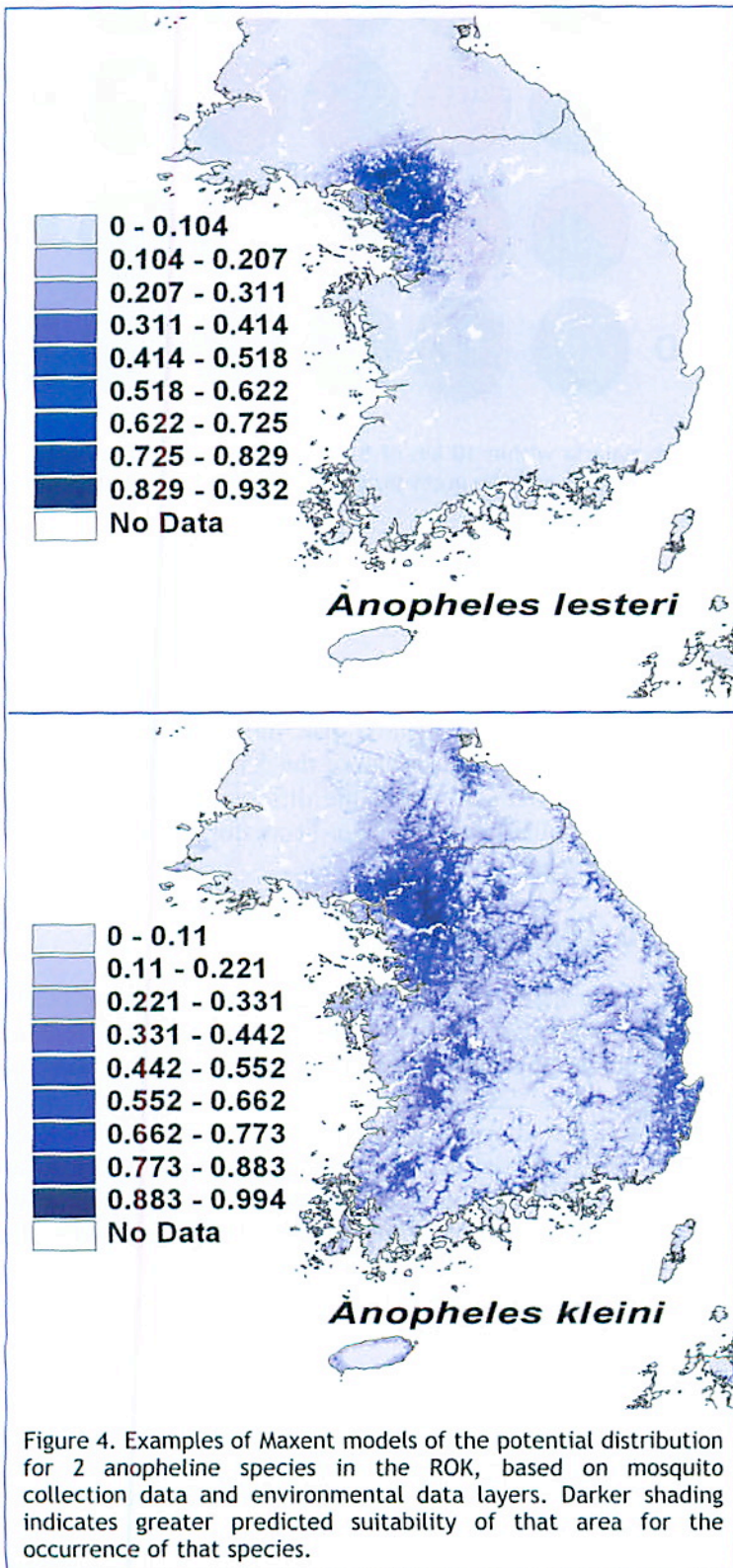
- altitude and a selection of climate grid layers for 1980 through 1990 from Worldclim,<sup>19</sup>
- five layers summarizing aspects of topography and landform (topographic index, slope, aspect, flow direction, and flow accumulation) from the US Geological Survey’s HYDRO-1K Elevation Derivative Database,<sup>20</sup>
- data layers summarizing the “greenness index”—termed the Normalized Difference Vegetation Index<sup>21</sup>—from the Advanced Very High Resolution Radiometer satellite data presenting percentage tree cover for 1992-1993,
- thirteen classes of land-use/land-cover from the Global Land Cover Facility,<sup>22</sup>
- soil taxonomy suborders of the world from the US Department of Agriculture National Soils Conservation Service,<sup>23</sup> and
- data on areas equipped for irrigation from the Aquastat site of the Food and Agriculture Organization of the United Nations.<sup>24</sup>



In all, 79 one-km<sup>2</sup> environmental data layers were available, which we reduced to 15 by principal components analysis (PCA) in Minitab 15.1.1.0

(Minitab Inc, State College PA) prior to mosquito distribution modelling. The 15 PC layers explained more than 95% of the overall variation in the 79 environmental parameters. We imported data into ArcView 3.3 (ESRI, Redlands, CA) for image analysis.

The current spatial limits of *P. vivax* in the ROK were taken from the MAP website<sup>10</sup> and resampled for one-km<sup>2</sup> resolution to match that of the mosquito distribution models (see Figure 2). We assumed that human population density throughout the areas of interest was sufficient for malaria transmission. We applied a 10-km radius buffer around 5 selected US military installations in the northeast of the ROK. Using ArcView 3.3, we conducted map queries for 3 scenarios for possible areas of coincidence of vectors and malaria within the buffers, where false=0 and true=1. We also conducted a map calculation for a fourth scenario where no coincidence of vectors and malaria=0, one vector species coinciding with malaria=1, two species coinciding=2, and three species coinciding with malaria=3. In scenario 1, only one species, *An. sinensis*, is considered a vector, as had been assumed by workers in the past. Scenario 2 assumes that any of the 8 anopheline species occurring in the ROK can transmit malaria if they co-occur with the spatial limits of parasites. This is the most conservative scenario. Scenario 3 assumes *An. kleini*, *An. pullus*, and *An. sinensis* are vectors, as has been suggested in the literature.<sup>13</sup> In this scenario the co-occurrence of any or all of these species with the malaria suitable area is scored as true (=1) for the purposes of the mal-area calculation. Scenario 4 assumes *An. kleini*, *An. pullus*, and *An. sinensis* are vectors, but that the risk increases if more than one species co-occurs with the malaria suitable area. These species were equally weighted, as definitive information on their relative vectorial importance is lacking. The total number of one-km<sup>2</sup> pixels scored true for the first 3 scenarios, and the sum of values for these pixels for the fourth scenario were calculated for the buffered areas surrounding the 5 installations.





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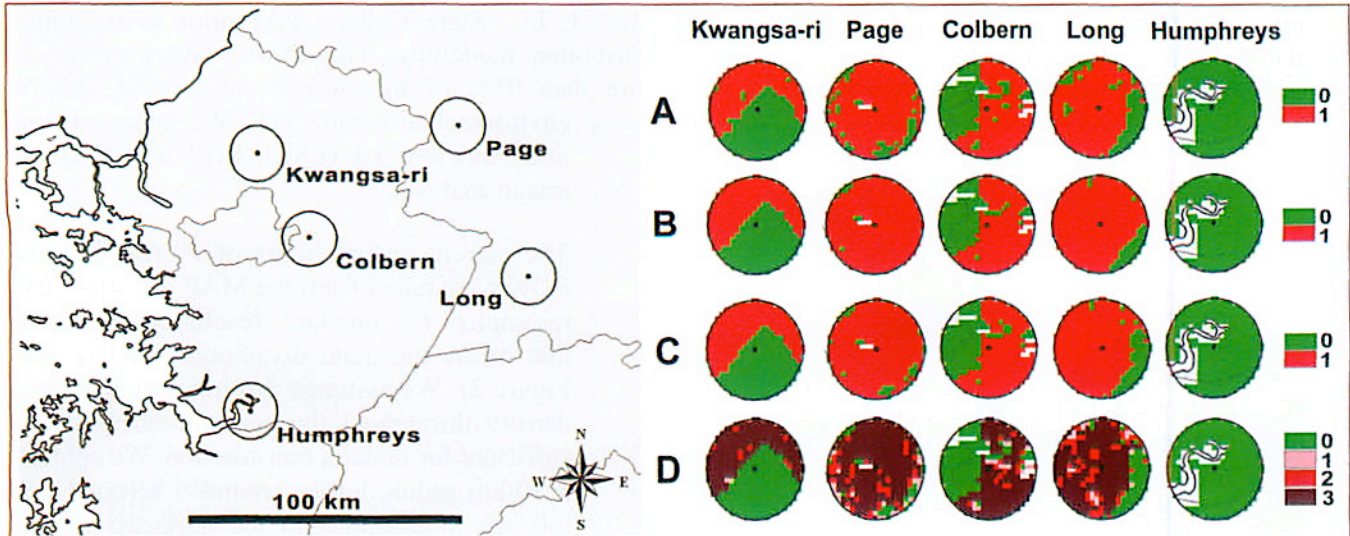


Figure 5. Four scenarios of the extent of the mal-area for malaria within 10 km of 5 US military installations in the ROK (one-km<sup>2</sup> pixel resolution), based on vector distribution models and the areas predicted suitable for malaria, from the Malaria Atlas Project.<sup>10</sup> Darker areas indicate greater risk of malaria.

### Legend:

- A. *Anopheles sinensis* is the only vector.
- B. Any of the 8 *Anopheles* species known from the ROK are present.
- C. Any of 3 species (*An. kleini*, *An. sinensis* and *An. pullus*) is present.

## RESULTS

Mosquitoes were identified to species from a total of 174 collection locations in the ROK from collections from 1998 through 2006 (see Figure 2). Some of these data were reported previously.<sup>25</sup> Distribution models revealed that *An. sinensis*, *An. kleini*, *An. pullus*, and *An. belenrae* were predicted to occur widely, whereas *An. lesteri* is predicted to occur only in northwest areas of the ROK (Figure 4). Examples of output from Maxent models for *An. kleini* and *An. lesteri* are presented in Figure 4. Collection data and distribution maps will be available from the MosquitoMap website\* and in a future publication. All species are predicted to occur in the north of the ROK where malaria has been most common since it first reappeared in 1993.

Mal-area calculations for the 4 scenarios are shown in Figure 5. In all scenarios, Camp Humphreys has no malaria transmission risk due to it falling outside the predicted spatial limits of malaria as given on the MAP website.<sup>10</sup> Comparison of the mal-area scores (Figure 6) reveals that Camp Humphreys and Kwangsa-ri have the lowest values. The scores for scenario 4 are higher than for the other scenarios,

reflecting the cumulative effect of vector species' occurrences on malaria risk. In these examples, the rank of the malaria risk of the 5 installations does not change markedly with the different scenarios, except that Colbern has a higher score for the *An. sinensis*-only scenario.

## DISCUSSION

Arthropod-borne infectious diseases are a major health threat to our combat troops. We cannot afford to ignore this health threat nor repeat the mistakes of previous conflicts where many Soldiers were debilitated or killed by preventable infectious diseases. Knowledge of the identity and occurrence of the major vectors is a prime requirement to determine the threat posed by vector-borne diseases. Predicting where the vectors are likely to be found could be a valuable addition to health risk assessment and disease control strategies.

As standardized and accessible techniques for modelling the distribution of disease vectors are recent developments, the approach given here is new. Application of models of vector distribution to disease risk assessment is a logical next step. We have shown that a simple index of the area where disease

\*<http://www.mosquitomap.org>



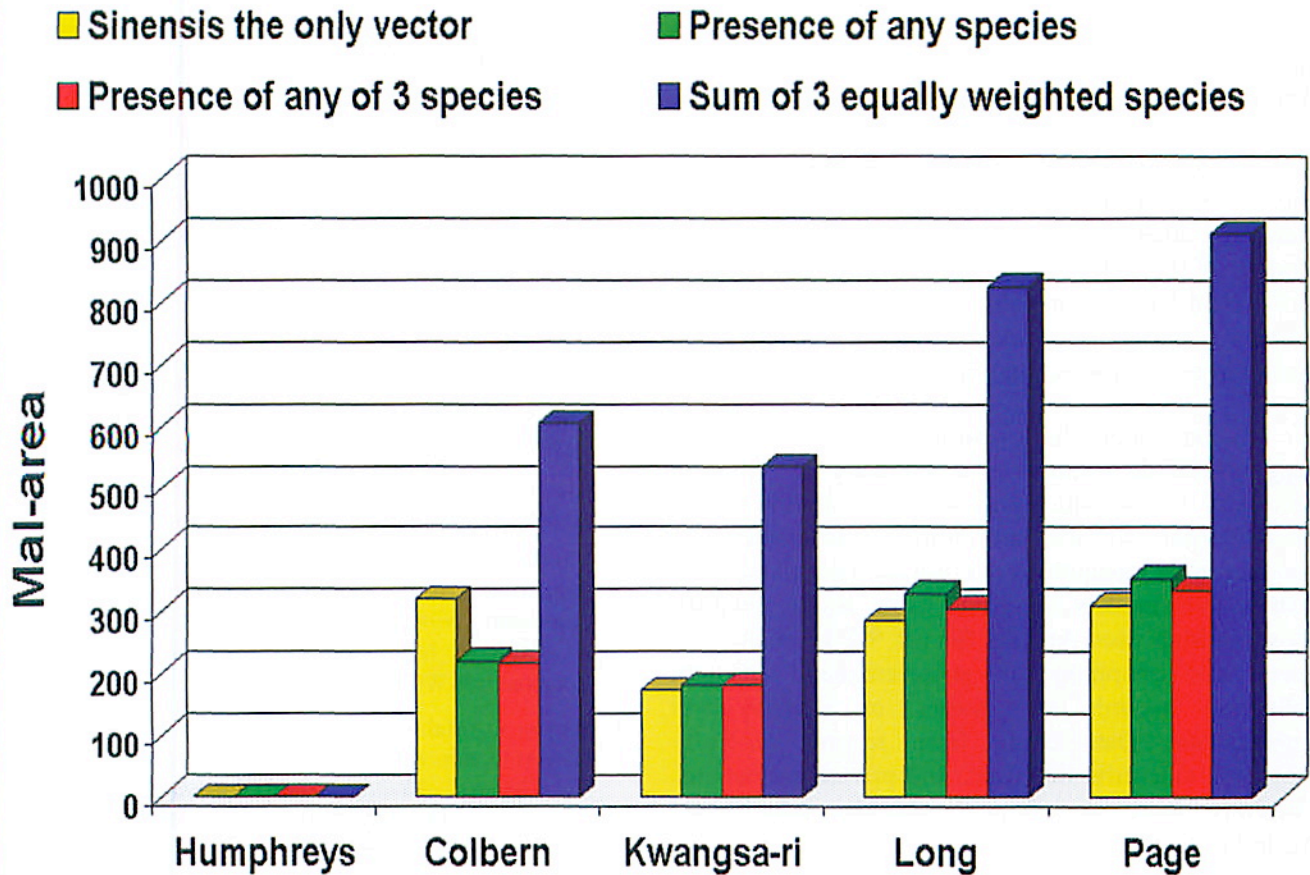


Figure 6. Mal-area calculations in number of one-km<sup>2</sup> pixels for malaria within 10 km of 5 US military installations in the ROK, based on vector distribution models and the areas predicted suitable for malaria, from the Malaria Atlas Project.

transmission is possible, the mal-area, can be used to assess disease risk for a 10 km radius buffer around US military installations in the ROK. Although any size area can be considered, a 10-km buffer is appropriate to calculate the health risk arising from the local environment, or the amount of vector control needed within a barrier zone around these points.

We have shown that the method of calculating the mal-area is an important variable. Identification of the vector species, and the weight attached to these species in terms of vectorial importance is also critical. However, the accuracy, scale, and precision of models of vector and parasite distribution is of fundamental importance. It should be noted that little information is available for malaria in North Korea<sup>11</sup> and so the malarious area may extend further north than shown here. The World Health Organization reported that a malaria epidemic occurred in North Korea shortly after the first case of malaria reemerged along the DMZ in

1993, suggesting a parallel outbreak occurred in both countries.<sup>26</sup> The mal-area calculations shown here do not yet take into account seasonality, use of insecticide bed nets, human movement, socio-economic level, or many other variables that modify the prevalence and incidence of malaria. In addition, vector distribution models predict general habitat suitability, but factors not included in these models include historical, physical, climatological, and biotic constraints that may play a role in limiting potential distribution. Evaluating and improving vector model accuracy is an ongoing task, but better models can be easily incorporated as they become available.

Despite the simplified assumptions of the mal-area method of risk assessment shown here, the approach is potentially very quick and can be used for any area of interest in the world, even where medical intelligence is sketchy. One can see the location of the mal-area within the area of interest, or the mal-area can be

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reduced to a single figure to compare risk between areas. In the absence of other intelligence, the mal-area approach has potential as a first approximation of risk. Alternatively, vector and mal-area maps can be used as base layers in more complex epidemiological GIS disease risk models. A generic mal-area tool could conceivably be used to measure any risk factor, including other vector-borne diseases, where spatial models of the risk components are available. Such a tool would have great value for medical intelligence estimates, particularly when forces are deployed to hostile locations for the first time.

We are constructing high resolution maps of potential geographical distribution of a selection of mosquito vectors of disease which will soon be available via the MosquitoMap website, an online clearinghouse for georeferenced mosquito collection records, and species distribution models derived from those records. MosquitoMap uses ArcGIS Server 9.2 to enable the query and mapping of georeferenced mosquito collection records as points or country-level aggregations. Data come from records held by museums, scientific literature, and private collections. Currently there are 65,000 records, mainly for Australasia and the Neotropics.

An application within MosquitoMap, the mal-area calculator, is designed to provide a fast, easy, and intuitive interface for rapidly assessing relative malaria risk. The intention is for the user to define a location or area anywhere on the face of the earth and the calculator combines models of disease distribution with predicted distribution of major disease vectors. Based on the location or area defined, an HTML and/or PDF chart will be rendered that graphs statistics for grid layers of various combinations of the VPH variables. These statistics will consist of the percentage of cells that contain a certain value for the user defined area. MosquitoMap and the mal-area calculator rely on distribution models for all vector species, but these are currently lacking. However, these applications provide a framework to host and analyze future vector and disease models as they become available.

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